

**CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION
PUBLIC REPORT 2007-8**

Active Ingredient: Nicarbazin
Tracking ID Number 218235

DESCRIPTION OF ACTION

Innolytics, LLC, submitted an application for California registration of OvoControl P, EPA Reg. No. 80224-1. OvoControl P is used to control feral pigeon populations by reducing egg hatchability. The product contains the active ingredient nicarbazin. Nicarbazin is a complex of two compounds, 1,3-bis (4-nitrophenyl) urea (DNC) and 4,6-dimethyl pyrimidin-2-ol (HDP).

The U.S. EPA registered OvoControl P conditionally on May 14, 2007. Under the conditions of registration, U.S. EPA requested a confirmatory efficacy field study and storage stability data and corrosion characteristics for OvoControl P.

DPR evaluated the OvoControl P label and data submitted by Innolytics, LLC, with their application for registration, and found them acceptable to support conditional registration. Precautionary and first aid statements and other protective measures on the product label adequately mitigate the potential health risks to users. DPR does not expect significant adverse environmental impacts to result from registration of OvoControl P.

BACKGROUND

Registrant:	Innolytics, LLC
Common name:	Nicarbazin
Chemical name:	1,3-bis (4-nitrophenyl) urea (DNC) 4,6-dimethyl pyrimidin-2-ol (HDP)
Brand name:	OvoControl P
Uses:	Reduce egg hatch
Pests controlled:	Feral pigeons
Type of registration:	Conditional Registration

OvoControl P consists of pellets ranging from 0.5 to 1 centimeter (cm) in diameter that contain 0.5 percent (%) nicarbazin. The active molecule in nicarbazin is DNC, which interferes with the formation of the vitelline membrane that separates the egg yolk from the egg white. Nicarbazin does not affect hormonal pathways. Researchers believe that the active ingredient interferes with cholesterol formation in the membrane, which prevents embryo formation. To produce the desired effect on egg hatchability, pigeons must eat the nicarbazin pellets for enough time, generally about seven days. Data show the effect is reversible. Once nicarbazin is removed from the diet, hatchability generally returns to normal in 7 to 14 days.

SCIENTIFIC REVIEW

A. Chemistry

1. **Product Chemistry:** DPR evaluated the submitted chemistry studies for OvoControl P. The product chemistry data support conditional registration of OvoControl P. The test results are summarized in Table 1. The conditional registration is contingent upon the submission of an acceptable 12-month storage stability and corrosion characteristics study for OvoControl P.

Table 1. Physical and Chemical Properties of Technical Nicarbazin	
Properties	Values
Physical state	Solid
Color	Light Yellow
Density (20 °C)	1.21 grams (gm)/cm ³
pH (1% solution)	5.0 – 7.0
Melting point	265 °C - 275 °C
Density	0.5 gm/cm ³
Partition coefficient (K _{ow})	DNC – 3,964 HDP – 0.116
Solubility	Slightly soluble in DMF & DMSO (polar apotic solvents)
Vapor pressure	Approaching zero
Storage stability	Not submitted
Corrosion characteristics	Not submitted

2. **Residues in Food and Animal Feed:** Innolytics, LLC, did not submit residue data. In accordance with California Notice 2004-7, these data are not required.
3. **Environmental Fate:** Innolytics, LLC, did not submit environmental fate data. Pursuant to the Pesticide Contamination Prevention Act of 1985, environmental fate data are not required for non-agricultural uses products as defined in the Food and Agricultural Code, section 11408. Submission of environmental fate data may be required for nicarbazin at a future date.

B. Toxicology

Innolytics, LLC, submitted adequate toxicology studies to conduct a complete toxicological evaluation of OvoControl P. The acute toxicity study data Innolytics, LLC, submitted was for Koffogran, which contains 25% nicarbazin. Koffogran is a feed additive intended for control of

coccidiosis, a debilitating protozoal infection in poultry. Koffogran was first used in 1955. Since the approval of nicarbazin by the Food and Drug Administration (FDA) in 1955, an estimated 10 million kilograms of nicarbazin has been fed to over 80 billion broiler chickens in the U.S. DPR determined that the Koffogran data are bridgeable for evaluation of OvoControl P.

In addition to the submitted studies, Innolytics, LLC, cited a rat acute oral LD₅₀ value for nicarbazin of greater than 10,000 mg/kg. Therefore, DPR determined that the acute oral and acute dermal studies for OvoControl P were not required. The acute inhalation toxicity study indicated a Category II toxicity hazard. However, because OvoControl is a granular material and the risk of inhalation exposure is minimal, DPR has accepted the Category III signal word, "Caution," on the OvoControl P label. The product label adequately identifies the potential acute toxicity hazards indicated by the data reviewed. The first aid statements and PPE are adequate for the indicated acute toxicity hazards. The acute toxicity parameters for OvoControl P are summarized in Table 3.

Table 3. Summary of Acute Toxicity of OvoControl P		
Type of Study	Acute Toxicity Values*	Acute Toxicity Category
Acute oral	Not submitted	N/A
Acute dermal	Not submitted	N/A
Acute inhalation	LC ₅₀ 0.147 mg/l	II
Primary eye irritation	Acceptable	III
Primary dermal irritation	Acceptable	IV
Dermal sensitization	Acceptable	Not a Sensitizer
Signal word	N/A	CAUTION
*Acute toxicity values expressed as: LD ₅₀ = Lethal dose that kills 50% of the test population LC ₅₀ = Lethal environmental concentration that kills 50% of the test population N/A = Not applicable		

DPR found the submitted toxicology studies for nicarbazin sufficient to satisfy the data requirements of the Birth Defects Prevention Act (Food and Agricultural Code section 13121, et al.). Of the submitted toxicology studies, the dog chronic toxicity study, and rat reproduction studies were unacceptable and not upgradeable. These were not upgradeable because they were conducted using protocols that did not meet present-day standards. The rat chronic toxicity and teratology studies were unacceptable and possibly upgradeable if additional data were submitted.

Despite these deficiencies, the available data was sufficient to determine that no adverse effects were evident and that the toxicity hazards from exposure to nicarbazin were minimal.

DPR prioritizes pesticide active ingredients for risk assessment based on of the nature the potential adverse health effects, the number of potential adverse effects, the number of species affected, no observable effect levels (NOELs), the potential for human exposure, use patterns, and other similar factors. Based on these criteria, pesticides with the greatest potential for health problems are placed in high priority, with other chemicals being in moderate or low priority. At this time, DPR has not prioritized nicarbazin for risk assessment. The purpose of the risk assessment would be to appraise the potential for nicarbazin to cause adverse health effects in humans if exposed to the pesticide through legal use. A summary of toxicology data with additional nicarbazin toxicity information is pending completion. Upon completion it will be available on the DPR public website at: <http://www.cdpr.ca.gov/docs/risk/toxsums/toxsumlist.htm>

C. Health & Safety

DPR's evaluation of the medical management information on the OvoControl P label and the acute toxicity study results indicate that the product label bears all of the required statements and warnings regarding safety to handlers and other persons who may be exposed to the pesticide. The product label bears an adequate First Aid statement. In addition, the product label requires handlers to wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. The instructions also direct handlers to wear protective eyewear, long sleeved shirt and long pants, socks, shoes and gloves.

D. Fish & Wildlife

The registrant submitted fish and wildlife toxicity studies, including studies on bobwhite quail, mallard duck, rainbow trout, bluegill sunfish, *Daphnia magna*, and earthworm. Toxicity studies were conducted with technical nicarbazin and its components DNC and HDP. The submitted data are adequate to characterize the toxicity to wildlife and aquatic animals from an environmental exposure. Table 4, on page 5, summarizes the results of these studies. The data indicate that nicarbazin is relatively non-toxic to birds, fish and *Daphnia magna*, and practically non-toxic to earthworms. Use of OvoControl P, according to its label, is restricted to flat rooftops and paved surfaces. To mitigate hazards to aquatic organisms, the OvoControl P label Environmental Hazards statement directs the user to not apply directly to water, or areas where surface water is present or to intertidal areas below the mean high water mark. When used as directed, DPR does not expect nicarbazin to be released into soil or waterways.

Table 4. Summary of Fish & Wildlife Toxicity Values*

Test Animal	Type of Study	Acute Toxicity Value**	Relative Toxicity
Bobwhite quail	Acute oral (nicarbazin)	>2250 mg/kg LD ₅₀	Relatively non-toxic
Bobwhite quail	Feeding (8 day) (nicarbazin)	>5625 ppm LC ₅₀ 320 ppm NOEC	Relatively non-toxic
Mallard duck	Feeding (8 day) (nicarbazin)	>5620 ppm LD ₅₀ 320 ppm NOEC	Relatively non-toxic
Rainbow trout	Water exposure (96 hrs) (HDP)	>110 ppm LC ₅₀	Relatively non-toxic
Rainbow trout	Water exposure (96 hrs) (DNC)	>96 ppb LC ₅₀	Practically non-toxic
Bluegill sunfish	Water exposure (96 hrs) (HDP)	>122 ppm LC ₅₀	Relatively non-toxic
Bluegill sunfish	Water exposure (96 hrs) (DNC)	>72 ppb LC ₅₀	Practically non-toxic
<i>Daphnia magna</i>	Water exposure (48 hrs) (HDP)	>107 ppm EC ₅₀ 107 ppm NOEC	Relatively non-toxic
<i>Daphnia magna</i>	Water exposure (48 hrs) (DNC)	>93 ppb EC ₅₀ 27 ppb NOEC	Practically non-toxic
Earthworm	Acute toxicity (14 day) (nicarbazin)	>1000 ppm LC ₅₀ 1000 ppm NOEC	Practically non-toxic

* The test substances used for the studies were technical nicarbazin and its components DNC and HDP, as indicated in the above studies

** Acute Toxicity Values expressed as:

LD₅₀ = Lethal dose that kills 50% of the test population

LC₅₀ = Lethal environmental concentration that kills 50% of the test population

EC₅₀ = Concentration of a toxicant causing a defined non-lethal effect in 50% of the test population

NOEC = No observed effect concentration

E. Efficacy

The hatchability effect of nicarbazin was originally reported by Merck in the early 1950's as an unwanted side effect in broiler breeder chickens. While nicarbazin has the same impact in all birds, each species requires a different dose to achieve the contraceptive effect. Pigeons are less

efficient in absorbing the compound and require a larger dose per body weight than other problem species such as geese. According to the OvoControl P label, each pigeon must consume a minimum of 0.1 ounces of OvoControl P per day. This dose equals 500 ppm nicarbazin per bird per day. In support of registration, Innolytics, LLC, submitted results of a feeding study in which fertility was measured in pigeons that were fed varying concentrations of the active ingredient (a.i.) nicarbazin over a 120 day test period. Test results demonstrated that 400 ppm a.i. reduced fertility 100%. DPR determined that the submitted data, as well as data in the public domain, were adequate to support registration of OvoControl P.

ALTERNATIVES

OvoControl P is used to reduce egg hatch in feral pigeons, and is formulated as a palatable bait, very similar to commercial pigeon feed. Feral pigeons are significant problems in urban and suburban environments. The costs of clean up, increased maintenance and transmission of disease to both livestock and humans are serious issues. Traditional mitigation methods for reducing feral pigeon populations have focused on exclusion, repellents, and toxicants. OvoControl P provides another means of controlling feral pigeons. OvoControl P is proven to significantly decrease the hatchability of eggs from pigeons fed OvoControl P daily during the nesting period. OvoControl P does not create a secondary toxicity hazard. The hatchability of eggs from a bird of prey, such as a falcon, that consumes treated pigeons will not be affected. When used in conjunction with traditional mitigation methods OvoControl P provides an effective integrated pest management strategy for control of feral pigeon populations.

CONCLUSION

DPR evaluated the product label and scientific data submitted to support the registration of OvoControl P. The label and data were found acceptable to support conditional registration. The acute health risks to human from exposure to nicarbazin are minimal due to its low mammalian toxicity. The precautionary and first aid statements on the product label, and the recommended protective measures mitigate potential health risks to persons who may be exposed to nicarbazin. If a DPR risk assessment finds that exposure to nicarbazin may result in unacceptable margins of exposure, further restrictions will be placed on the use of nicarbazin at that time. Conditional registration of OvoControl P is recommended for one year pending the submission of an acceptable 12-month storage stability and corrosion characteristics study. If Innolytics, LLC, does not submit the required data within one year, the registration for OvoControl P will not be renewed.